Claims

1. An isolated peptide of *Cry j* I or an isolated portion thereof, said peptide or portion thereof comprising at least one T cell epitope of *Cry j* I, said peptide having an amino acid sequence selected from the group consisting of CJ1-2, CJ1-3, CJ1-4, CJ1-7, CJ1-8, CJ1-9, CJ1-10, CJ1-11, CJ1-12, CJ1-14, CJ1-15, CJ1-16, CJ1-17, CJ1-18, CJ1-19, CJ1-20, CJ1-21, CJ1-22, CJ1-23, CJ1-24, CJ1-25, CJ1-26, CJ1-27, CJ1-30, CJ1-31, CJ1-32 and CJ1-35.

2. An isolated peptide or portion thereof of claim 1 wherein said portion of said peptide has a mean T cell stimulation index equivalent to or greater than the mean T cell stimulation index of said peptide as shown in Fig. 14.

3. An isolated peptide or portion thereof of claim 1 which comprises at least two T cell epitopes.

4. An isolated peptide or portion thereof of claim 1 which, when administered to an individual sensitive to Japanese cedar pollen, induces T cell anergy in the individual or modifies the lymphokine secretion profile of T cells in the individual.

5. A portion of an isolated peptide of claim 1 which has a mean T cell stimulation index of at least 2.0.

6. All or a portion of an isolated peptide of claim 1 which does not bind immunoglobulin E specific for *Cry j* I in a substantial percentage of individuals sensitive to *Cry j* I, or if binding of the peptide or portion thereof to said immunoglobulin E occurs, such binding does not result in release of mediators from mast cells or basophils in a substantial percentage of individuals sensitive to *Cry j* I.

7. An isolated peptide of claim 1 which binds immunoglobulin E to a substantially lesser extent than *Cry j* I binds immunoglobulin E.

8. All or a portion of an isolated peptide of claim 1 which modifies in an individual sensitive to Japanese cedar pollen to whom it is administered, the allergic response of the individual to a Japanese cedar pollen.

9. A portion of an isolated peptide of claim 1 wherein the portion comprises at least 15 amino acid residues.

10. An isolated nucleic acid sequence having a sequence encoding all or a portion of a peptide of claim 1, or the functional equivalent of said nucleic acid sequence.

11. An isolated peptide which is immunologically cross-reactive with antibodies specific for all or a portion of a peptide of claim 1.

12. An isolated peptide which is immunologically cross-reactive with T cells reactive with all or a portion of a peptide of claim 1.

13. An isolated peptide or portion thereof of Japanese cedar pollen protein allergen,*Cry j* I, said peptide or portion thereof comprising at least one T cell epitope of said protein allergen, said peptide having a positivity index of at least about 100 and mean T cell stimulation index of at least about 3.5 determined in a population of individuals sensitive to said protein allergen.

14. An isolated peptide or portion thereof of claim 13 wherein said population of individuals is at least seventeen individuals.

15. An isolated peptide or portion thereof of claim 14 wherein said population of individuals is at least thirty individuals.

16. An isolated peptide or portion thereof of claim 14 wherein said mean T cell stimulation index is at least about 5.0.

17. An isolated peptide or portion thereof of claim 14 wherein said mean T cell stimulation index is at least about 7.0.

18. A peptide or portion thereof of claim 14 wherein said peptide is selected from the group consisting of: CJ1-9, CJ1-10, CJ1-16, CJ1-17, CJ1-20, CJ1-22, CJ1-23, CJ1-24, CJ1-27, CJ1-30, CJ1-31, CJ1-32 and CJ1-35.

19. A peptide or portion thereof of claim 17 wherein said peptide has an amino acid sequence selected from the group consisting of: CJ1-10, CJ1-16, CJ1-17, CJ1-20, CJ1-22, CJ1-27 and CJ1-32.

20. A modified peptide or a modified portion of a peptide of claim 1.

21. A modified peptide or a modified portion of a peptide of claim 20 which does not bind immunoglobulin E specific for *Cry j* I in a substantial percentage of individuals sensitive to *Cry j* I, or if binding of the peptide or portion thereof to said immunoglobulin E occurs, such binding does not result in release of mediators from mast cells or basophils in a substantial percentage of individuals sensitive to *Cry j* I.

22. A modified peptide or a modified portion of a peptide of claim 20 which modifies, in an individual sensitive to Japanese cedar pollen to whom it is administered, the allergic response of the individual to a Japanese cedar pollen allergen.

23. An isolated peptide of *Cry j* I or portion thereof comprising amino acids 151-352 of the amino acid sequence of *Cry j* I as shown in Fig. 4a - b.

24. A modified peptide or a modified portion of a peptide of claim 23.

25. An isolated peptide comprising at least two regions, each region comprising at least one T cell epitope of *Cry j* I, said regions each comprising all or a portion of an amino acid sequence selected from the group consisting of: CJ1-1, CJ1-2, CJ1-3, CJ1-4, CJ1-7, CJ1-8, CJ1-9, CJ1-10, CJ1-11, CJ1-12, CJ1-14, CJ1-15, CJ1-16, CJ1-17, CJ1-18, CJ1-19, CJ1-20, CJ1-21, CJ1-22, CJ1-23, CJ1-24, CJ1-25, CJ1-26, CJ1-27, CJ1-28, CJ1-30, CJ1-31, CJ1-32, CJ-33, CJ-34 and CJ1-35.

26. All or a portion of an isolated peptide of claim 25 wherein said regions comprise an amino acid sequence selected from the group consisting of: CJ1-9, CJ1-10, CJ1-16, CJ1-17, CJ1-20, CJ1-22, CJ1-23, CJ1-24, CJ1-27, CJ1-30, CJ1-31, CJ1-32, CJ1-35.

27. An isolated peptide of claim 25, wherein said peptide comprises a combination of regions selected from the group consisting of:

CJ1-1, CJ1-2 and CJ1-3;
CJ1-1 and CJ1-2;
CJ1-9 and CJ1-10;
CJ1-14, CJ1-15, CJ1-16 and CJ1-17;
CJ1-20, CJ1-21, CJ1-22, CJ1-23;
CJ1-20, CJ1-22 and CJ1-23;
CJ1-22 and CJ1-23;
CJ1-22, CJ1-23 and CJ1-24;
CJ1-30, CJ1-31 and CJ1-32;
CJ1-31 and CJ1-32;
CJ1-22, CJ1-23, CJ1-16 and CJ1-17;
CJ1-22, CJ1-23, CJ1-31 and CJ1-32;
CJ1-16, CJ1-17, CJ1-31 and CJ1-32;
CJ1-9, CJ1-10 and CJ1-16;
CJ1-17, CJ1-22 and CJ1-23;
CJ1-16, CJ1-17 and CJ1-20;

CJ1-31, CJ1-32 and CJ1-20;
CJ1-22, CJ1-23, CJ1-1, CJ1-2 and CJ1-3;
CJ1-16, CJ1-17, CJ1-22 and CJ1-23, CJ1-31 and CJ1-32;
CJ1-9, CJ1-10, CJ1-16, CJ1-17, CJ1-22 and CJ1-23;
CJ1-9, CJ1-10, CJ1-16, CJ1-17, CJ1-31 and CJ1-32;
CJ1-9, CJ1-10, CJ1-22, CJ1-23, CJ1-31 and CJ1-32;
CJ1-9, CJ1-10, CJ1-16, CJ1-17, CJ1-22, CJ1-23, CJ1-31 and CJ1-32;
CJ1-1, CJ1-2, CJ1-16, CJ1-17, CJ1-22 and CJ1-23.

28. An isolated nucleic acid having a sequence encoding said isolated peptide or portion thereof of claim 1 or the functional equivalent of said nucleic acid sequence.

29. An isolated peptide produced in a host cell transformed with the nucleic acid of claim 28.

30. An isolated nucleic acid having a sequence encoding a peptide of claim 25, or the functional equivalent of said nucleic acid sequence.

31. An isolated peptide produced in a host cell transformed with the nucleic acid of claim 30.

32. All or a portion of an isolated peptide of *Cry j* I, said peptide or portion thereof comprising at least one T cell epitope of said protein allergen, said peptide having the formula X_n-Y-Z_m, wherein Y is an amino acid sequence selected from the group consisting of: CJ1-2, CJ1-3, CJ1-4, CJ1-7, CJ1-8, CJ1-9, CJ1-10, CJ1-11, CJ1-12, CJ1-14, CJ1-15, CJ1-16, CJ1-17, CJ1-18, CJ1-19, CJ1-20, CJ1-21, CJ1-22, CJ1-23, CJ1-24, CJ1-25, CJ1-26, CJ1-27, CJ1-28, CJ1-30, CJ1-31, CJ1-32 and CJ1-35 wherein X_n are amino acid residues contiguous to the amino terminus of Y in the amino acid sequence of said protein allergen, wherein Z_m are amino acid residues contiguous to the carboxy terminus of Y in the amino acid sequence of said protein allergen,

wherein n is 0-30 and wherein m is 0-30.

33. A portion of an isolated peptide of claim 32 wherein the portion comprises at least fifteen amino acid residues.

34. All or a portion of an isolated peptide of claim 32 which does not bind immunoglobulin E specific for *Cry j* I in a substantial percentage of individuals sensitive to the protein allergen, or if binding of the peptide or portion thereof to said immunoglobulin E occurs, such binding does not result in release of mediators from mast cells or basophils in a substantial percentage of individuals sensitive to the protein allergen.

35. An isolated peptide or portion thereof of claim 32 which binds immunoglobulin E to a substantially lesser extent than *Cry j* I binds said immunoglobulin E.

36. An isolated peptide of *Cry j* I or an isolated portion thereof, said peptide or portion thereof comprising at least one T cell epitope of *Cry j* I, said peptide having an amino acid sequence comprising amino acids 20-324 or 341-353 of *Cry j* I as shown in Fig. 4a-b.

37. A therapeutic composition comprising at least one isolated peptide or a portion thereof of claim 1 and a pharmaceutically acceptable carrier or diluent.

38. A therapeutic composition comprising at least one isolated peptide or portion thereof of claim 13 and a pharmaceutically acceptable carrier or diluent.

39. A therapeutic composition comprising an isolated peptide or portion thereof of claim 23 and a pharmaceutically acceptable carrier or diluent.

40. A method of treating sensitivity to Japanese cedar pollen allergen or an allergen which is immunologically cross-reactive with Japanese cedar pollen allergen in an individual, comprising administering to the individual a therapeutically effective amount of the composition of claim 37.

41. A method of treating sensitivity to Japanese cedar pollen allergen or an allergen which is immunologically cross-reactive with Japanese cedar pollen allergen in an individual, comprising administering to the individual a therapeutically effective amount of the composition of claim 39.

42. A method of treating sensitivity to Japanese cedar pollen allergen or an allergen which is immunologically cross-reactive with Japanese cedar pollen allergen in an individual, comprising administering simultaneously or sequentially to the individual a therapeutically effective amount of at least two different compositions of claim 37.

43. A method of treating sensitivity to Japanese cedar pollen allergen or an allergen which is immunologically cross-reactive with Japanese cedar pollen allergen in an individual, comprising administering simultaneously or sequentially to the individual a therapeutically effective amount of at least two different compositions of claim 38.

44. A method of detecting sensitivity to Japanese cedar pollen in an individual, comprising combining a blood sample obtained from the individual with at least one peptide of claim 1, under conditions appropriate for binding of blood components with the peptide, and determining the extent to which such binding occurs as indicative of sensitivity in the individual to Japanese cedar pollen.

45. A method of claim 44 wherein the extent to which binding occurs is determined by assessing T cell function, T cell proliferation or a combination thereof.

46. A method of detecting sensitivity to Japanese cedar pollen in an individual, comprising combining a blood sample obtained from the individual with at least one peptide of claim 13, under conditions appropriate for binding of blood components with the peptide, and determining the extent to which such binding occurs as indicative of sensitivity in the individual to Japanese cedar pollen.

47. A method of claim 46 wherein the extent to which binding occurs is determined by assessing T cell function, T cell proliferation or a combination thereof.

48. A method of detecting sensitivity to Japanese cedar pollen in an individual, comprising combining a blood sample obtained from the individual with all or a portion of at least one peptide of claim 32, under conditions appropriate for binding of blood components with the peptide or portion thereof, and determining the extent to which such binding occurs as indicative of sensitivity in the individual to Japanese cedar pollen.

49. A method of claim 48 wherein the extent to which binding occurs is determined by assessing T cell function, T cell proliferation or a combination thereof.

50. A therapeutic composition comprising a pharmaceutically acceptable carrier or diluent and at least two peptides, said peptides each comprising at least one T cell epitope of *Cry j* I.

51. A composition of claim 50 wherein said peptides are selected from the group consisting of: CJ1-1, CJ1-2, CJ1-3, CJ1-4, CJ1-7, CJ1-8, CJ1-9, CJ1-10, CJ1-11, CJ1-12, CJ1-14, CJ1-16, CJ1-17, CJ1-18, CJ1-19, CJ1-20, CJ1-21, CJ1-22, CJ1-23, CJ1-24, CJ1-25, CJ1-26, CJ1-27, CJ1-28, CJ1-30, CJ1-31, CJ1-32, CJ1-33, CJ1-34 and CJ1-35 and wherein said composition comprises a sufficient percentage of the T cell epitopes of said protein allergen such that

upon administration of the composition to an individual sensitive to a Japanese cedar pollen allergen, T cells of the individual are tolerized to said at least one protein allergen.

52. A composition of claim 51 comprising a combination of peptides selected from the group consisting of:

CJ1-1, CJ1-2 and CJ1-3;
CJ1-1 and CJ1-2;
CJ1-9 and CJ1-10;
CJ1-14, CJ1-15, CJ1-16 and CJ1-17;
CJ1-20, CJ1-21, CJ1-22, CJ1-23;
CJ1-20, CJ1-22 and CJ1-23;
CJ1-22 and CJ1-23;
CJ1-22, CJ1-23 and CJ1-24;
CJ1-30, CJ1-31 and CJ1-32;
CJ1-31 and CJ1-32;
CJ1-22, CJ1-23, CJ1-16 and CJ1-17;
CJ1-22, CJ1-23, CJ1-31 and CJ1-32;
CJ1-16, CJ1-17, CJ1-31 and CJ1-32;
CJ1-9, CJ1-10 and CJ1-16;
CJ1-17, CJ1-22 and CJ1-23;
CJ1-16, CJ1-17 and CJ1-20;
CJ1-31, CJ1-32 and CJ1-20;
CJ1-22, CJ1-23, CJ1-1, CJ1-2 and CJ1-3;
CJ1-16, CJ1-17, CJ1-22 and CJ1-23, CJ1-31 and CJ1-32;
CJ1-9, CJ1-10, CJ1-16, CJ1-17, CJ1-22 and CJ1-23;
CJ1-9, CJ1-10, CJ1-16, CJ1-17, CJ1-31 and CJ1-32;
CJ1-9, CJ1-10, CJ1-22, CJ1-23, CJ1-31 and CJ1-32;
CJ1-9, CJ1-10, CJ1-16, CJ1-17, CJ1-22, CJ1-23, CJ1-31 and CJ1-32; and
CJ1-1, CJ1-2, CJ1-16, CJ1-17, CJ1-22 and CJ1-23.

53. A method of treating sensitivity to Japanese cedar pollen allergen or an allergen which is immunological cross-reactive with Japanese cedar pollen allergen in an individual, comprising administering to the individual a therapeutically effective amount of the composition of claim 50.

54. A method of treating sensitivity to Japanese cedar pollen allergen or an allergen which is immunologically cross-reactive with Japanese cedar pollen allergen in an individual, comprising administering to the individual a therapeutically effective amount of the composition of claim 52.

55. A therapeutic composition comprising at least one peptide of *Cry j* I and a pharmaceutically acceptable carrier or diluent, said composition comprising a sufficient percentage of the T cell epitopes of *Cry j* I such that upon administration of the composition to an individual sensitive to a Japanese cedar pollen allergen, T cells of the individual are tolerized to *Cry j* I.

56. A method of treating sensitivity to Japanese cedar pollen allergen or an allergen which is immunologically cross-reactive with Japanese cedar pollen allergen in an individual, comprising administering to the individual a therapeutically effective amount of a composition of claim 55.

57. A nucleic acid sequence coding for the Japanese cedar pollen allergen *Cry j* I, or at least one fragment thereof or the functional equivalent of said nucleic acid sequence.

58. A nucleic acid sequence of claim 57 wherein said nucleic acid sequence consists essentially of at least one fragment of the coding portion of the nucleic acid sequence of *Cry j* I as shown in Fig. 4 a-b.

59. A host cell transformed to express a protein or peptide encoded by the nucleic acid sequence of claim 57.

60. Isolated Japanese cedar pollen allergen *Cry j* I or at least one antigenic fragment thereof produced in a host cell transformed with the nucleic acid sequence of claim 57.

61. Isolated Japanese cedar pollen allergen *Cry j* I or at least one antigenic fragment thereof of claim 60 wherein said allergen or fragment thereof does not bind immunoglobulin E specific for Japanese cedar pollen or if binding of the Japanese cedar pollen allergen to said immunoglobulin E occurs, such binding does not result in histamine release from mast cells or basophils.

62. The isolated allergen or antigenic fragment of claim 60 wherein said isolated allergen or said antigenic fragment is capable of modifying, in a Japanese cedar pollen-sensitive individual to which it is administered, the allergic response to Japanese cedar pollen.

63. A method of producing Japanese cedar pollen allergen *Cry j* I or at least one fragment thereof comprising the steps of:

a) culturing a host cell transformed with a nucleic acid sequence encoding Japanese cedar pollen allergen *Cry j* I or fragment thereof in a appropriate medium to produce a mixture of cells and medium containing said Japanese cedar pollen allergen *Cry j* I or at least one fragment thereof; and

b) purifying said mixture to produce substantially pure Japanese cedar pollen allergen *Cry j* I, or at least one fragment thereof.

64. An isolated antigenic fragment of *Cry j* I wherein said antigenic fragment does not bind immunoglobulin E specific for Japanese cedar pollen or if binding of the fragment to said immunoglobulin E occurs, such binding does not result in histamine release from mast cells or basophils.

65. A modified Japanese cedar pollen allergen which, when administered to a Japanese cedar pollen-sensitive individual, reduces the allergic response of the individual to Japanese cedar pollen allergen.

66. At least one modified fragment of Japanese cedar pollen allergen, which when administered to a Japanese cedar pollen-sensitive individual, reduces the allergic response of the individual to Japanese cedar pollen allergen.

67. An isolated protein allergen or antigenic fragment thereof that is immunologically related to *Cry j* I or fragment thereof.

68. A therapeutic composition comprising isolated Japanese cedar pollen allergen *Cry j* I or at least one fragment thereof and a pharmaceutically acceptable carrier or diluent.

69. A protein preparation comprising Japanese cedar pollen allergen *Cry j* I, or at least one fragment thereof synthesized in a host cell transformed with a nucleic acid sequence encoding all or a portion of Japanese cedar pollen allergen *Cry j* I.

70. A method of treating sensitivity to Japanese cedar pollen allergen or an allergen immunologically cross-reactive with Japanese cedar pollen allergen in a mammal sensitive to said allergen, comprising administering to said mammal a therapeutically effective amount of said preparation of claim 69.

71. A method of detecting sensitivity in a mammal to a Japanese cedar pollen allergen comprising combining a blood sample obtained from said mammal with a purified Japanese cedar pollen allergen or antigenic fragment thereof produced in a host cell transformed with the nucleic acid sequence of claim 57 or chemically synthesized under conditions appropriate for binding of blood components with the protein or fragment thereof and determining the extent to which such binding occurs.

72. A method of detecting sensitivity of a mammal to Japanese cedar pollen allergen comprising administering to said mammal a sufficient quantity of the Japanese cedar pollen allergen *Cry j* I or at least one antigenic fragment thereof produced in a host cell transformed with the nucleic acid sequence of claim 57 or chemically synthesized to provoke an allergic response in said mammal and determining the occurrence of an allergic response in the individual to said Japanese cedar pollen allergen or antigenic fragment thereof.

73. A monoclonal antibody specifically reactive with a Japanese cedar pollen allergen, *Cry j* I, or at least one antigenic fragment thereof.

74. All or a portion of an isolated peptide of *Cry j* I, said peptide or portion thereof comprising at least one T cell epitope of *Cry j* I, said peptide having an amino acid sequence selected from the group consisting of amino acid residues 1-40, amino acid residues 81-110, amino acid residues 151-180, amino acid residues 191-240 and amino acid residues 291-330 of *Cry j* I as shown in Fig. 4a-b.

75. A method of designing antigenic fragments of *Cry j* I, which when administered to Japanese cedar pollen sensitive individuals in sufficient quantity will modify the individual's allergic exposure to Japanese cedar pollen comprising the steps of:

(a) recombinantly or synthetically producing peptides of *Cry j* I;

(b) examining said peptides for their ability to influence B cell and/or T cell responses in Japanese cedar pollen sensitive individuals; and

(c) selecting appropriate peptides which contain epitopes recognized by the cells.